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The CO₂ Dissociation Curve at Steady State in Vivo

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ABSTRACT

The CO₂ content in blood ([CO₂]) depends not only on PCO₂, but also on the O₂ saturation ([SO₂]). Since SO₂ changes in parallel with [CO₂] in capillary blood ([CO₂]^{*}) at steady state, the slope of [CO₂]^{*} against PCO₂ becomes steeper than that of [CO₂] measured in oxygenated or deoxygenated blood. In the preceding paper it was made clear that the change in [CO₂] due to that in SO₂ (*i.e.*, the Haldane effect, [CO₂]_{HE}) became proportional to the respiratory quotient (RQ). Since the ratio of the arterial-venous (a-v) difference in SO₂ (*av* [SO₂]) to that in [CO₂]^{*} (*av* [CO₂]^{*}) was in inverse proportion to the RQ, the ratio of the a-v difference in [CO₂]_{HE} (*av* [CO₂]_{HE}) to *av* [CO₂]^{*} became constant irrespective of the RQ. Designating the PCO₂ dependent component of [CO₂] except for [CO₂]_{HE} by [CO₂]_P, the ratio *av* [CO₂]_P/*av* [CO₂]^{*} also became constant. Thus, using [CO₂]_P measured in oxygenated blood *in vitro*, [CO₂]^{*} could be expressed by an exponential function of PCO₂.

Key words : Carbonic anhydrase, O₂ saturation, Haldane effect, Respiratory quotient, \dot{V}_a/\dot{Q} ratio

INTRODUCTION

The change in CO₂ content [CO₂] in blood occurs mainly on the active site of carbonic anhydrase, which is present not only in the red blood cell, but also in the capillary endothelium¹⁾. When [CO₂] and [H⁺] change at

the active site due to the changes in PCO₂ and O₂ saturation ([SO₂]), respectively, changes in carbamate and bicarbonate concentration take place²⁾. Designating the change in [CO₂] resulting from the change in SO₂ (*i.e.*, the Haldane effect) by [CO₂]_{HE} and that resulting from the change in PCO₂ by [CO₂]_P, the change in [CO₂] in capillary blood ([CO₂]^{*}) is given by

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the sum of changes in $[\text{CO}_2]_{\text{HE}}$ and $[\text{CO}_2]_{\text{P}}$.

Basically, $[\text{CO}_2]_{\text{HE}}$ is the difference in $[\text{CO}_2]$ between oxygenated and deoxygenated blood^{(3),(4)} and the arterial-venous (a-v) difference in $[\text{CO}_2]_{\text{HE}}$ ($a_v[\text{CO}_2]_{\text{HE}}$) is given by multiplying $[\text{CO}_2]_{\text{HE}}$ by the a-v difference in SO_2 ($a_v[\text{SO}_2]$). $a_v[\text{SO}_2]$ is given by dividing the a-v difference in O_2 content ($a_v[\text{O}_2]$) by the O_2 capacity (CapO_2). The a-v difference in $[\text{CO}_2]^*$ ($a_v[\text{CO}_2]^*$) is derived by multiplying $a_v[\text{O}_2]$ by the respiratory quotient (RQ). Hence, the ratio $a_v[\text{SO}_2]/a_v[\text{CO}_2]^*$ is given by $1/(\text{RQ} \cdot \text{CapO}_2)$. In the preceding paper it was clarified that $[\text{CO}_2]_{\text{HE}}$ at the steady state became proportional to the RQ (see Eq. 29) and the ratio $a_v[\text{CO}_2]_{\text{HE}}/a_v[\text{CO}_2]^*$, which was given by multiplying $[\text{CO}_2]_{\text{HE}}$ by $a_v[\text{SO}_2]/a_v[\text{CO}_2]^*$, became constant⁽⁵⁾. Therefore, the ratio of the a-v difference in $[\text{CO}_2]_{\text{P}}$ ($a_v[\text{CO}_2]_{\text{P}}$) to $a_v[\text{CO}_2]^*$ also becomes constant irrespective of RQ, PCO_2 and SO_2 .

$[\text{CO}_2]_{\text{P}}$ had been measured in oxygenated blood and expressed by an exponential function of PCO_2 ⁽⁴⁾. Thus, $[\text{CO}_2]^*$ could be approximated from the ratio $a_v[\text{CO}_2]_{\text{P}}/a_v[\text{CO}_2]^*$ by a definite exponential function of PCO_2 . The change in carbamate concentration in the red cell is included in $[\text{CO}_2]_{\text{HE}}$, and therefore, the ratio $a_v[\text{CO}_2]_{\text{HE}}/a_v[\text{CO}_2]^*$ becomes higher than that of the a-v difference in Haldane effect component of $[\text{HCO}_3^-]$ in plasma ($[\text{HCO}_3^-]_{\text{HE}}$) to that in $[\text{HCO}_3^-]$ measured ($[\text{HCO}_3^-]^*$) (see Eq. 19 in the preceding paper)⁽⁵⁾. Thus, it is imperative to apply $[\text{CO}_2]^*$ to analyze the gas exchange rate at the steady state.

THEORETICAL DERIVATION OF THE FUNCTION FOR $[\text{CO}_2]^*$

As written in the preceding paper $[\text{HCO}_3^-]_{\text{HE}}$ was proportional to the RQ at steady state as

given by $2.09 \cdot \text{RQ}^{(5)}$. $[\text{HCO}_3^-]$ in plasma was expressed by the molar concentration. Taking the mean of plasma volume in blood (1 - Hct) to be 0.544 over the PCO_2 range of 30 to 70 mmHg, the molar unit in plasma is converted to vol% in blood by multiplying 0.544×2.226 . In addition, the ratio $[\text{HCO}_3^-]_{\text{HE}}/[\text{CO}_2]_{\text{HE}}$ was 0.386 over the physiological PCO_2 range⁽⁴⁾. Hence, $[\text{CO}_2]_{\text{HE}}$ was rewritten as follows:

$$[\text{CO}_2]_{\text{HE}} = 6.555 \cdot \text{RQ} \cdot (\text{vol}\%). \quad (1)$$

$[\text{CO}_2]_{\text{HE}}$ measured in tonometered blood was about 5.9 vol% and agreed well with $[\text{CO}_2]_{\text{HE}}$ of Eq. (1) when $\text{RQ} = 0.9^{(4),(5)}$. As described in the Introduction, the ratio $a_v[\text{SO}_2]/a_v[\text{CO}_2]^*$ was given by

$$(-) a_v[\text{SO}_2]/a_v[\text{CO}_2]^* = 1/(\text{RQ} \times \text{CapO}_2). \quad (2)$$

Taking CapO_2 to be 20 vol%, the ratio $a_v[\text{CO}_2]_{\text{HE}}/a_v[\text{CO}_2]^*$ is written from Eqs. (1) and (2) as

$$a_v[\text{CO}_2]_{\text{HE}}/a_v[\text{CO}_2]^* = 0.328. \quad (3)$$

Since $a_v[\text{CO}_2]_{\text{P}} = a_v[\text{CO}_2]^* - a_v[\text{CO}_2]_{\text{HE}}$, the ratio $a_v[\text{CO}_2]_{\text{P}}/a_v[\text{CO}_2]^*$ is expressed as follows:

$$a_v[\text{CO}_2]_{\text{P}}/a_v[\text{CO}_2]^* = 0.672. \quad (4)$$

The CO_2 content obtained in oxygenated blood⁽⁴⁾ was given by

$$[\text{CO}_2]_{\text{P}} = 8.748 \cdot \text{PCO}_2^{0.435}, (\text{vol}\%). \quad (5)$$

Assuming $[\text{CO}_2]_{\text{P}}$ of Eq. (5) to be equal to $[\text{CO}_2]^*$ at 40 mmHg PCO_2 , the difference in $[\text{CO}_2]^*$ between any PCO_2 and 40 mmHg can be

CO₂ Dissociation Curve at Steady State

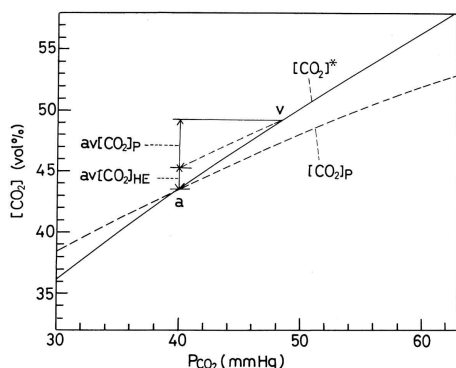


Fig. 1 .

$[\text{CO}_2]^*$ (solid line; Eq.6) and $[\text{CO}_2]_P$ (broken line; Eq.5) plotted against PCO_2 . The and show the venous and arterial PCO_2 levels. The vertical segment at PaCO_2 shows the a-v difference in $[\text{CO}_2]^*$, $[\text{CO}_2]_P$ and $[\text{CO}_2]_{\text{HE}}$.

calculated from Eqs. (4) and (5). $[\text{CO}_2]^*$ is then numerically plotted against PCO_2 . The solid line in Fig.1 shows $[\text{CO}_2]^*$ and the broken line $[\text{CO}_2]_P$ of Eq. (5). Furthermore, from the relationship between PCO_2 and $[\text{CO}_2]^*$, $[\text{CO}_2]^*$ was approximated by the following equation:

$$[\text{CO}_2]^* = 4.208 \cdot \text{PCO}_2^{0.632}, (\text{vol}\%). \quad (6)$$

$[\text{CO}_2]^*$ of Eq. (6) agreed with $[\text{CO}_2]_P$ of Eq. (5) at 41.04 mmHg PCO_2 , and the ratio $\text{av}[\text{CO}_2]_P / \text{av}[\text{CO}_2]^*$ was 0.709 at 30 mmHg PCO_2 and decreased to 0.651 at 70 mmHg PCO_2 .

In the PCO_2 range of 30 to 70 mmHg, the mean ratio was 0.678 ± 0.018 .

DISCUSSION

$[\text{CO}_2]^*$ of Eq. (6) is very important to estimate $\text{av}[\text{CO}_2]^*$ from the a-v difference in PCO_2 . The points a and v in Fig. 1 indicate the arterial and venous PCO_2 levels. The vertical segment at PaCO_2 indicates $\text{av}[\text{CO}_2]^*$. The magnitude of $\text{av}[\text{CO}_2]_{\text{HE}}$ was about a half that

of $\text{av}[\text{CO}_2]_P$, irrespective of the PCO_2 range. If $\text{av}[\text{CO}_2]$ were estimated from the a-v difference in PCO_2 by using Eq. (5), it will be greatly underestimated.

The relationship between $\text{av}[\text{CO}_2]^*$ and $\text{av}[\text{O}_2]$ was further calculated, using the relationship of alveolar ventilation to pulmonary blood flow (\dot{V}_A/\dot{Q}) as follows⁽⁶⁾:

$$\dot{V}_A/\dot{Q} = 8.63 \cdot \text{RQ} \cdot \text{av}[\text{O}_2]/\text{PaCO}_2 \quad (7)$$

Calculated data are shown in Fig.2, where PaCO_2 was taken to be 41 mmHg and $[\text{O}_2]$ (vol%) in arterial blood was derived from the alveolar air equation⁽⁶⁾, assuming $[\text{O}_2]$ was fully saturated with alveolar PO_2 . The solid lines indicate the change in $[\text{CO}_2]^*$ along the three RQ values. Since PaCO_2 was taken to be constant, $\text{av}[\text{CO}_2]^*$ was unrelated to the RQ, but increased with an increase in \dot{V}_A/\dot{Q} ratio. When the \dot{V}_A/\dot{Q} ratio was 0.85, $\text{av}[\text{CO}_2]^*$ was about 4 vol%. The broken lines show $\text{av}[\text{CO}_2]_{\text{HE}}$ calculated from Eq. (3), these were about 33% $\text{av}[\text{CO}_2]^*$ regardless of the RQ and \dot{V}_A/\dot{Q} ratio.

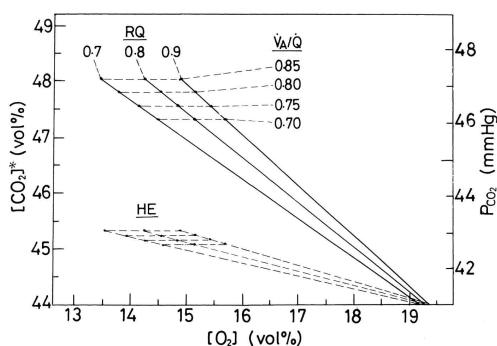


Fig. 2 .

The relationship between the a-v differences in $[\text{O}_2]$ and $[\text{CO}_2]^*$. $[\text{O}_2]$ and $[\text{CO}_2]^*$ at the arterial level were calculated from the alveolar air equation, and those at venous level were obtained from the equation for the \dot{V}_A/\dot{Q} ratio⁽⁶⁾. shows $[\text{CO}_2]_{\text{HE}}$ calculated from Eq. (3).

Figure 2 shows that, when P_{aCO_2} is constant, $[CO_2]^*$ and venous P_{CO_2} are defined only by the \dot{V}_A/\dot{Q} ratio. This well controlled relationship will be ascribed to the interaction of the catalytic reaction rates of carbonic anhydrase in the red blood cell and the capillary endothelium.

The scale on the right ordinate shows P_{CO_2} given by Eq. (6). Since $[CO_2]_{HE}$ includes the change in carbamate concentration in the RBC⁽⁴⁾, the ratio $[CO_2]_{HE}/[CO_2]^*$ of Eq. (3) (0.328) was about 30% greater than the ratio $[HCO_3^-]_{HE}/[HCO_3^-]^*$ (0.252)⁽⁵⁾. If the a-v difference in P_{CO_2} were estimated from $[CO_2]^*$ by using Eq. (5), the change in P_{CO_2} will be greatly overestimated.

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